REMARKS

Claims 46-98 are all the claims pending in the application. Applicants have canceled claims 19-32, 34 and 36-45 and have added new claims 51-98, which depend from claims 46-50 and correspond to claims 20-32, 34 and 36-45. In addition, Claims 46 and 48 have been amended to properly recite Markush language. Further, claims 48-50 have been amended to delete the term "unevenly" for purposes of clarity. Entry of the above amendments is respectfully requested.

Preliminarily, Applicants would like to thank the Examiner and her supervisor for the personal interview conducted with Applicants' representatives on September 13, 2000. Applicants believe that the interview was helpful in advancing the prosecution of the present application.

I. Objection and Rejection under 35 U.S.C. § 112, first paragraph

On page 2 of the Office Action, the Examiner objects to the amendment filed on March 14, 2001 under 35 U.S.C. § 132 because it allegedly introduces new matter into the disclosure of the invention. The Examiner asserts that the new matter is the phrase "the drug is unevenly dispersed on or in the water-absorbing and water-insoluble base material" in claim 48.

In addition, on page 3 of the Office Action, the Examiner rejects claims 48-50 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts that Applicants have not pointed out support for "the drug is unevenly dispersed on or in the water-

absorbing and water-insoluble base material".

Applicants have amended claims 48-50 by deleting the term "unevenly" in line 18, as discussed during the interview with the Examiner, for purposes of clarity. Accordingly, Applicants respectfully request that the objection and rejection be withdrawn.

II. Response to rejection of claims 32, 46 and 47 under 35 U.S.C. § 112, second paragraph

On pages 3-4 of the Office Action, the Examiner rejects claims 32, 46 and 47[2] under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants respectfully traverse this rejection for the following reasons.

Applicants respectfully submit that the phrase "insulin-like growth factor" is a term of art that is well-known by a person of skill in the art. Accordingly, Applicants submit herewith pages from *Products for Life Science Research* to support Applicants' position that the phrase "insulin-like growth factor" is a term of art. Accordingly, Applicants respectfully submit that a person of skill in the art would understanding the meaning and scope of the claims.

With respect to claims 46 and 48, Applicants have amended the claims to properly recite Markush language.

In view of the above, Applicants respectfully request that the objection and

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[2] It is Applicants' understanding that the Examiner meant claim 48, not claim 47.

rejections be withdrawn.

III. Rejection of claims 19-32, 34 and 36-50 under 35 U.S.C. § 102/103

Claims 19-26, 28-32, 34 and 36-50 are rejected under 35 U.S.C. § 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Suzuki et al. (U.S. Patent 4,613,500). The Examiner's position is substantially the same as in the previous Office Actions.

The Examiner believes that Suzuki discloses that the drug is dispersed more on or in the water-absorbing and water-insoluble base material than on or in the water-absorbing and gel-forming base material because Suzuki discloses that the drug is adhered to or dispersed in the water-absorbing and water-insoluble base material at col. 5, lines 53-66. However, the passage pointed out by the Examiner appears to be directed to a composition where only a water-absorbing and water-insoluble base material is used. Therefore, Applicants submit that the disclosure is not directed to a composition that contains a water-absorbing and water-soluble base material, and that when a water-absorbing and water-soluble base material is added, the drug adheres more to the water-absorbing and water-soluble base material.

In this regard, Applicants direct the Examiner's attention to the Declaration under 37 C.F.R. § 1.132 submitted herewith to demonstrate the difference between the present invention and Suzuki, and that as a result, the present invention provides unexpectedly superior results.

As discussed in the Declaration, Suzuki discloses three methods for forming a composition when a water-absorbing and water-soluble base material is used. First, at column 6, line 39-43, Suzuki discloses that "it may be admixed with polypeptide or its

derivative and a water-absorbing and water-insoluble base in the mechanical mixing process, followed by the above-mentioned processes of compacting, etc." When the water-absorbing and water-insoluble base material and water-absorbing and water-soluble base material are mixed simultaneously, the strength of mixing influences the amount of drug that adheres to the water-absorbing and water-insoluble base. In order for more of the drug to adhere to the water-absorbing and water-insoluble base, strong mixing is required. However, Suzuki does not teach or suggest the strength of mixing.

Therefore, Suzuki does not teach or suggest a process of making a composition where more drug adhered to the water-absorbing and water-insoluble base material than on the water-absorbing and water-soluble base material. In particular, Suzuki does not teach or suggest a process that provides a composition having more drug adhered to the water-absorbing and water-insoluble base material than on the water-absorbing and water-soluble base material where 60% or more of the drug is adhered to the water-absorbing and water-insoluble base material. Therefore, the composition produced by the above Suzuki process is fundamentally different from the composition of the present invention

Second, at column 6, line 43-46, Suzuki discloses that "a water-absorbing and water-soluble base may be introduced into the process wherein polypeptide or its derivative is mixed with a water-absorbing and water-insoluble base in the presence of water." In the presence of water, the drug adheres more to the water-absorbing and water-soluble base because polypeptides drugs are hydrophilic and dissolve in water, and the water-absorbing and water-soluble base dissolves in water while the water-absorbing and water-insoluble base does not dissolve in water. Accordingly, the

composition produced by this method does not have more drug adhered to the water-absorbing and water-insoluble base material than on or in the water-absorbing and water-soluble base material. In addition, the composition of Suzuki does not have 60% or more of the drug adhered to the water-absorbing and water-insoluble base material. Therefore, the composition produced by the above Suzuki process is fundamentally different from the composition of the present invention.

Third, at column 6, line 49-53, Suzuki discloses that "wherein a water-absorbing and water-soluble base is added to polypeptide or its derivative in the process in which polypeptide or its derivative is to be freeze-dried, thus both components being freeze-dried simultaneously as mentioned above." In this case, since the drug is freeze-dried with the water-absorbing and water-soluble base material, the drug adheres more to the water-absorbing and water-soluble base than on or in the water-absorbing and water-insoluble base material. Therefore, the composition produced by the above Suzuki process is fundamentally different from the composition of the present invention.

Since the compositions of Suzuki and the present invention are fundamentally different and since the compositions are made by different processes, Applicants respectfully submit that Suzuki does not teach or suggest the present invention.

In addition, Applicants submit that there is no motivation for a person of ordinary skill in the art to mix to obtain uneven distribution of the drug more on or in the water-absorbing and water-insoluble base material than on or in the water-absorbing and gel-forming base material, as presently claimed. Although the Examiner asserts that the motivation to do so is the desire of obtaining efficient absorption of

the drug by nasal administration, Suzuki fails to include any disclosure concerning an embodiment in which the drug adheres more on or in the water-absorbing and water-insoluble base than on or in the water-absorbing and gel-forming base when both bases are present. Therefore, a person of ordinary skill in the art would not be motivated to obtain such a composition.

Furthermore, the present invention attains significantly higher amount of drug absorption and high maximum plasma concentration (Cmax) than the composition of Suzuki, as shown in the Declaration under 37 C.F.R. § 1.132 submitted on March 14, 2001. Accordingly, the present invention provides unexpectedly superior results over Suzuki.

In view of the above, Applicants respectfully submit that Suzuki fails to teach or suggest the composition of the present invention, and respectfully requests that the rejection be reconsidered and withdrawn.

IV. Response to rejection of claim 27 under 35 U.S.C. § 103

On pages 7-8 of the Office Action, the Examiner rejects claim 27 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Suzuki et al. in view of Makino et al. (U.S. Patent 5,262,871). The Examiner's position is substantially the same as in the previous Office Actions.

Applicants respectfully traverse this rejection for the following reasons.

Initially, Applicants submit that claim 27 has been canceled. However, Applicants submit that claims 58 and 82, which correspond to original claim 27, should be allowed at least for the reason that Suzuki does not teach or suggest the present invention, as discussed above. In addition, Makino et al. does not make up for

the deficiencies of Suzuki because Makino does not teach or suggest a powdery composition where a drug is unevenly dispersed more on or in a water-absorbing and water-insoluble base material than on or in a water-absorbing and gel-forming base material. Therefore, Suzuki in view of Makino fail to teach or suggest the present invention.

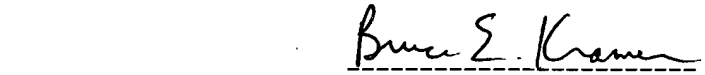
Accordingly, Applicants respectfully request that the rejection be withdrawn.

V. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicants hereby petition for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,



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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 19-32, 34 and 36-45 are canceled.

The claims have been changed as follows.

46. (amended) A powdery composition for nasal administration wherein

(1) the composition contains

(i) a drug,

(ii) one or more of a water-absorbing and gel-forming base material selected from the group consisting of hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose, hydroxyethyl cellulose, and sodium carboxymethyl cellulose and

(iii) one or more of a water-absorbing and water-insoluble base material selected from the group consisting of crystalline cellulose, α-cellulose, cross-linked sodium carboxy-methyl cellulose, cross-linked starch, chitin and chitosan,

(2) the content of the water-absorbing and gel-forming base material is about 5-40 wt% based on the total of the water-absorbing and water-insoluble base material and the water-absorbing and gel-forming base material, and

(3) the drug is unevenly dispersed more on or in the water-absorbing and water-insoluble base material than on or in the water-absorbing and gel-forming base material, and

wherein 70 wt % or more based on the drug is dispersed on or in the water-

absorbing and water-insoluble base material and on or in the water-absorbing and gel-forming base material.

48. (amended) A powdery composition for nasal administration wherein

(1) the composition contains

(i) a drug,

(ii) one or more of a water-absorbing and gel-forming base material selected from the group consisting of hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methyl cellulose, hydroxyethyl cellulose, and sodium carboxymethyl cellulose and

(iii) one or more of a water-absorbing and water-insoluble base material selected from the group consisting of crystalline cellulose, α-cellulose, cross-linked sodium carboxy-methyl cellulose, cross-linked starch, chitin and chitosan,

(2) the content of the water-absorbing and gel-forming base material is about 5-40 wt% based on the total of the water-absorbing and water-insoluble base material and the water-absorbing and gel-forming base material, and

(3) the drug is unevenly dispersed more on or in the water-absorbing and water-insoluble base material than on or in the water-absorbing and gel-forming base material,

wherein 60 wt % or more based on the drug is [unevenly] dispersed on or in the water-absorbing and water-insoluble base material.

49. (amended) The powdery composition according to claim 48, wherein 70 wt % or more based on the drug is [unevenly] dispersed on or in the water-absorbing and water insoluble base material.

50. (amended) The powdery composition according to claim 48, wherein 80 wt % or more based on the drug is [unevenly] dispersed on or in the water-absorbing and water insoluble base material.

Claims 51-98 are added as new claims.